AMENDMENTS TO THE SPECIFICATION

Please insert the following paragraph below the title of the invention:

This application is a national phase entry of PCT Application No. PCT/EP03/02611, filed on March 13, 2003, which claims the benefit under 35 U.S.C § 119(a)-(d) or (f) of German Patent Application No. DE 1021063.8, filed on March 13, 2002, each of which is incorporated by reference herein in its entirety including all figures and tables.

Please replace the paragraph bridging pages 65 and 66 with the following rewritten paragraph:

In this example, the feasibility in principle of the protease switch on the membrane in PC12 20.4 cells is described. It was the aim to establish a further intracellular mechanism which transduces proteolytic events at the periphery into permanent signals. For this purpose, the Gal4/VP16 fusion protein required for recombinase activation was anchored on the membrane (TM-GV) and was then intended to activate via a specific proteolytic cleavage the reporter system in the nucleus. Stable localization of Gal4/VP16 on the cell membrane was achieved by fusion to the transmembrane domain of the PDGF (platelet derived growth factor) receptor, with insertion and correct orientation of the construct in the membrane being ensured by an N-terminal signal sequence. The efficacy of activation was analyzed via expression of the EGFP reporter. For this purpose, the transfected cells were trypsinated after 48 h and the proportion of positive cells was quantitatively determined in an FAC analyzer (FACSCalibur from BD Bioscience). For this experiment, in each case 1.5×10^5 PC12 20.4 cells were plated on a 24-well plate and transfected with in each case 0.5 μg of the corresponding plasmid DNA on the next day (Lipofectamine2000; Invitrogen). Transient expression of the chimeric membrane protein in PC12 20.4 cells resulted in no significant activation of the reporter system (Fig. 15), demonstrating that the GV transcription activator is stably anchored on the membrane. To proteolytically remove the GV transactivator, the bases coding for the 7 amino acid recognition sequence (ENLYFQG) **(SEQ ID NO: 1)** of the tobacco etch virus (TEV) Nla protease (TEV protease) were inserted into the DNA sequence between PDGF transmembrane segment and Gal4/VP16. Introduction of this or alternative

protease cleavage sites did not result in any unspecific release of the Gal4/VP16 fusion protein. Coexpression of the TEV protease, however, led to efficient cleavage of the TM/tev/GV construct and subsequently to distinct activation of the Cre/EGFP reporter system. In another step, it was intended to demonstrate that the TEV protease is active even after membrane anchoring. The latter is a basic requirement for the interaction analysis of membrane proteins. For this purpose, the TEV protease was, analogously to the Gal4/VP16 reporter, N-terminally fused to the transmembrane domain of the PDGF receptor and coexpressed with the TM/tevS/GV construct in PC12 20.4 cells. The result showed no significant difference in the activation of the Cre/EGFP reporter system by soluble and membrane-bound protease. This example underlines the suitability in principle of the method of detecting protein interactions outside the nucleus, in particular on the cell membrane. A precondition for this is the functional coupling of an interaction to the proteolytic cleavage, and this may be carried out by transcomplementation of a protease or, in the case of a low concentration of the partners involved, also by producing a suitable proximity between protease and cleavage site (Fig. 15).